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DOI: https://doi.org/10.1016/j.gdata.2014.02.002

Genomics Data 2 (2014) 42–43

Contents lists available at ScienceDirect

Genomics Data

journal homepage: http://www.journals.elsevier.com/genomics-data/

Data in Brief

Genome-wide profiling to analyze the effects of high fat diet induced obesity on renal gene expression in mouse with reduced renal mass

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ARTICLE INFO

Article history:
Received 16 February 2014
Received in revised form 19 February 2014
Accepted 20 February 2014
Available online 2 March 2014

Keywords:
High fat diet
Gene regulation
Chronic kidney failure
Microarray

ABSTRACT

To assess the relationship between a reduced nephron number and a particular susceptibility to obesity-induced renal damage, mice underwent uninephrectomy (UNX) followed by either normal chow or high-fat diet (HFD) and were compared with sham-operated control mice. Analysis of gene expression in the mouse kidney by whole genome microarrays indicated that high fat diet led to more changes in gene expression than uninephrectomy. However, the combination of UNX and HFD additionally altered the effects of obesity on gene expression pattern. Here we describe in details the contents and quality controls for the gene expression and related results associated with the data uploaded to Gene Expression Omnibus (accession number GSE53996).

Specifications	
Organism/cell line/tissue	*Mus musculus*/kidney
Strain(s)	C57/BJ
Sex	Male
Sequencer or array type	Agilent-026655 Mouse GE 4x44K v2
Data format	Raw data: TXT files, normalized data: TXT
Experimental factors	Sham vs. UNX, chow vs. HFD
Experimental features	A unique microarray dataset of high fat diet induced mouse nephropathy model
Consent	All protocols were approved by the Cantonal Veterinary Office in Zurich
Sample source location	Zurich, Switzerland

Direct link to deposited data

Deposited data can be found here: http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE53996.

Experimental design, materials and methods

Uninephrectomy and kidney function data

Male C57/BJ mice aged 6 weeks were randomly assigned to uninephrectomy (UNX) or sham procedures and fed with a high fat diet (D12331; ResearchDiets, NJ, USA) or control chow diet (Provimi Kliba). Mice were divided into 4 groups of 6: Sham-chow, UNX-chow, sham-HFD and UNX-HFD. For uninephrectomy, the left kidney was surgically removed via a left paramedian incision on the back under anesthesia. The adrenal gland was carefully freed from the upper pole of the renal capsule before the renal pedicle was ligated and the kidney removed. For sham surgery, the kidney was manipulated without ablation. All mice were sacrificed under anesthesia 20 weeks after surgery and the kidneys were harvested. Half of the kidney from each animal was snap frozen in liquid nitrogen and stored at −80 °C for RNA and protein extraction. All protocols conformed to the Swiss animal protection laws and were approved by the Cantonal Veterinary Office in Zurich, Switzerland. Kidney functions of the different treatment groups are checked and described in Table 1. Both urine albumin/creatinine ratio and urine H_2O_2/creatinine level are increased in mice fed with HFD for 20 weeks. Moreover, albumin and H_2O_2 levels were significantly higher in the UNX group after 20 weeks of the high fat diet, indicating much severer kidney damages in such a treatment group.

Microarray and gene expression analysis

RNA was extracted from the frozen kidney using RNeasy Microarray Tissue mini kit (73304, Qiagen, Germany), followed by column DNase digestion to remove any contaminating genomic DNA. RNA samples from 4 mice per group were subjected to microarray analysis. Briefly, 100 ng of total RNA was reverse-transcribed into double-stranded cDNA, which was linearly amplified and labeled with Cy3 dye. Following quantification using a Nanodrop spectrophotometer (Witec, Luzern, Switzerland) and quality assessment with Agilent 2100 Bioanalyzer

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http://dx.doi.org/10.1016/j.gdata.2014.02.002

Table 1
Baseline markers for kidney function from the different treatment groups.

	Sham		UNX	
	Chow	HFD	Chow	HFD
Urinary albumin/creatinine ratio (mg/g)	46.9 ± 15.1	728 ± 177.2*	49.4 ± 18.8	1206 ± 260.4*,§
Urinary H_2O_2/creatinine ratio (nmol/mg)	109.5 ± 69.6	370.2 ± 20.2*	83.0 ± 49.7	584.1 ± 50.9*,§

Abbreviations: UNX, uninephrectomy; HFD, high fat diet. n = 6–8 mice/group. Data are shown as mean ± SEM.
* $p < 0.05$, comparison between chow and HFD.
§ $p < 0.05$, comparison between sham and UNX.

(Agilent Technologies, Santa Clara, CA), 1.6 μg of the obtained Cy3-labeled cRNA was hybridized to Mouse GE 4x44K v2 Microarrays (Agilent Technologies, Santa Clara, CA) according to the manufacturer's protocol. Arrays were scanned with an Agilent G2565CA Microarray Scanner System (Agilent, Santa Clara, CA). Raw intensity data were obtained using Agilent's Feature Extraction Software version 10.7 for array image analysis and the calculation of spot intensity measurements. All microarray data were submitted to the Gene Expression Omnibus [1] (accession number GSE53996).

Normalization

Data analysis was carried out with R/Bioconductor [2]. The processed intensities and normalized across samples were loaded by using quantile normalization implemented in the Bioconductor package preprocessCore [3]. Differential expression was computed using the limma package [4]. More details on analysis methods can be found at http://fgcz-bfabric.uzh.ch/wiki/tiki-index.php?page=app.two_groups.

Table 2
Microarray analysis of mRNA expression levels in kidney tissue of the four treatment groups.

Cooperation between groups	Number of differentially expressed genes
UNX-chow vs. sham-chow	157
UNX-HFD vs. sham-HFD	136
Sham-HFD vs. sham-chow	2441
UNX-HFD vs. UNX-chow	2581

Summary of differentially expressed genes between groups. Cut off 1.7-fold, $p < 0.05$.

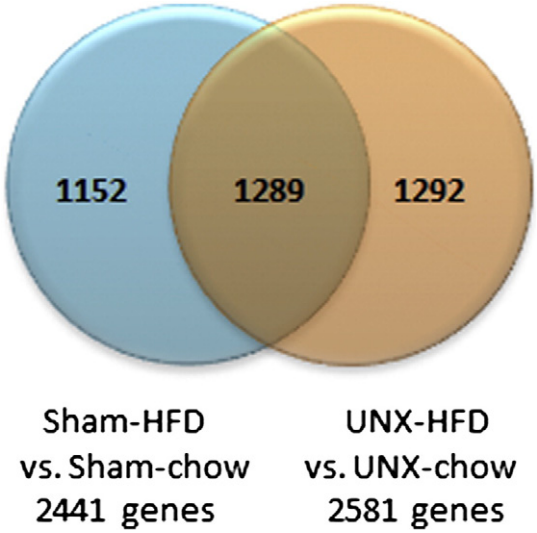

Fig. 1. Comparison of common and distinct gene expression patterns across the different experimental conditions. The Venn diagram analysis of sham versus UNX datasets indicates that 1289 genes (overlapped) are commonly expressed in both the sham-HFD and UNX-HFD kidneys, whereas 1152 and 1292 genes are distinctly expressed in the sham-HFD kidneys (blue) or UNX-HFD kidneys (orange), respectively. Data were analyzed using Subio platform software.

Basic analysis

First, gene expression was compared between UNX-chow mice versus sham-chow mice (UNX-chow/sham-chow) and between UNX-HFD mice versus sham-HFD mice (UNX-HFD/sham-HFD). By using a ≥1.7-fold change as a cut-off, only 157 genes were differentially expressed between the UNX-chow/sham-chow groups and 136 genes between the UNX-HFD/sham-HFD groups (Table 2). Next, in order to identify the genes altered by HFD, the following datasets were compared: UNX-HFD versus UNX-chow (designated as UNX dataset) and sham-HFD versus sham-chow (designated as sham dataset). Comparison of data from sham-HFD versus sham-chow and data from UNX-HFD versus UNX-chow revealed that 2441 and 2581 genes, respectively, were significantly increased or decreased at least 1.7-fold (Table 2).

Interestingly, a substantial number of genes (1289 genes) overlapped in being differentially expressed in both the UNX-HFD/UNX-chow and the sham-HFD/sham-chow datasets, as shown by the Venn diagram analysis [5] (Fig. 1). The overlapping genes in both of the UNX and sham datasets indicate that these genes are universally changed by high fat diet. However, the genes showed an altered expression only in the UNX-HFD remnant kidneys which suggests that these genes are changed by the synergetic effects of obesity and uninephrectomy (Fig. 1 orange part). Further analysis on the genes differentially expressed in between different groups revealed that more genes related with nephropathy were uniquely expressed in the UNX-HFD dataset. Moreover, genes implicated in renal hypoxia showed an altered expression only in the UNX-HFD remnant kidneys. The altered expression of genes responsive to hypoxia is consistent with the increased urinary H_2O_2 levels in UNX-HFD mice.

Discussion

We described here a unique dataset of mouse kidney disease model with obesity. This dataset is composed of genome-wide gene expression profiling data measured by Agilent platform. We showed that obesity induced proteinuria and oxidative stress in mice fed a HFD, and these changes were further enhanced by uninephrectomy. Furthermore, gene-profiling analysis of differentially expressed genes in the kidneys from each group revealed the synergistic effects of UNX and HFD on the gene expression levels. As a consequence, the function of the remnant kidney is more severely impaired.

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